

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	64	CDDO	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/11/07 11:34
L2	5	CDDO-Me	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/11/07 11:34
L3	3	I1 and @ad<"20001128"	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/11/07 11:37
L4	8	"KONOPLEVA, MARINA".in. or "ANDREEFF, MICHAEL".in. or "SPORN, MICHAEL"".in. "	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2007/11/07 11:38

09/998,009

11/7/2007

## Connecting via Winsock to STN

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TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 4 JUL 02 CHEMCATS accession numbers revised  
NEWS 5 JUL 02 CA/CAplus enhanced with utility model patents from China  
NEWS 6 JUL 16 CAplus enhanced with French and German abstracts  
NEWS 7 JUL 18 CA/CAplus patent coverage enhanced  
NEWS 8 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification  
NEWS 9 JUL 30 USGENE now available on STN  
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NEWS 12 AUG 13 CA/CAplus enhanced with additional kind codes for granted patents  
NEWS 13 AUG 20 CA/CAplus enhanced with CAS indexing in pre-1907 records  
NEWS 14 AUG 27 Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB  
NEWS 15 AUG 27 USPATOLD now available on STN  
NEWS 16 AUG 28 CAS REGISTRY enhanced with additional experimental spectral property data  
NEWS 17 SEP 07 STN AnaVist, Version 2.0, now available with Derwent World Patents Index  
NEWS 18 SEP 13 FORIS renamed to SOFIS  
NEWS 19 SEP 13 INPADOCDB enhanced with monthly SDI frequency  
NEWS 20 SEP 17 CA/CAplus enhanced with printed CA page images from 1967-1998  
NEWS 21 SEP 17 CAplus coverage extended to include traditional medicine patents  
NEWS 22 SEP 24 EMBASE, EMBAL, and LEMBASE reloaded with enhancements  
NEWS 23 OCT 02 CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt  
NEWS 24 OCT 19 BEILSTEIN updated with new compounds  
  
NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.  
  
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FILE 'HOME' ENTERED AT 11:41:16 ON 07 NOV 2007

=> file registry  
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:41:28 ON 07 NOV 2007  
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DICTIONARY FILE UPDATES: 6 NOV 2007 HIGHEST RN 952567-23-6

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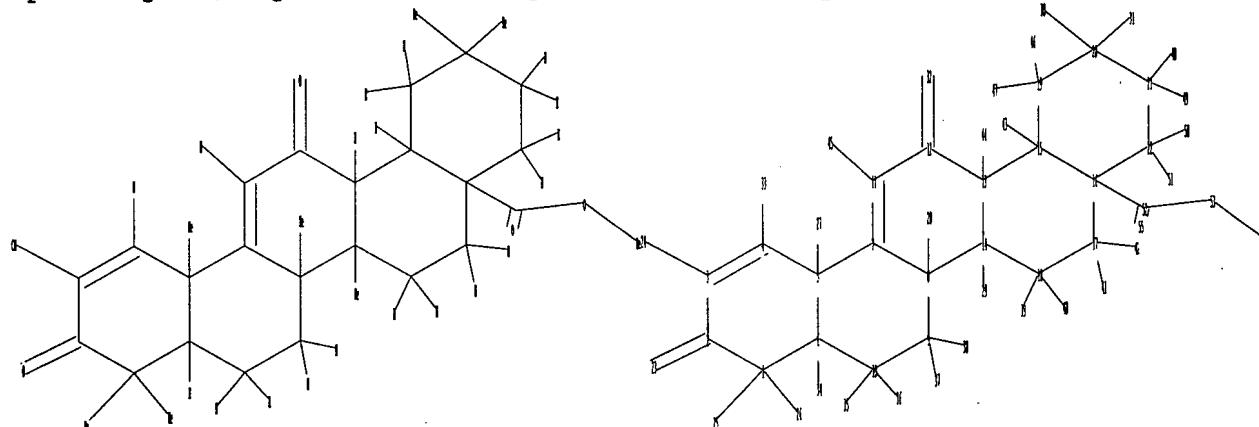
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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<http://www.cas.org/support/stngen/stndoc/properties.html>

```
=> Uploading C:\Program Files\Stnexp\Queries\09998009_cddome_2.str
```



```

chain nodes :
23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43
44 45 46 47 48 49 50 51 52 53 54 55
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
chain bonds :
1-25 1-26 2-23 3-24 4-33 5-27 6-34 8-28 9-37 9-38 10-35 10-36 11-45
12-32 13-44 14-29 15-43 16-52 17-41 17-42 18-39 18-40 19-46 19-47 20-30
20-31 21-48 21-49 22-50 22-51 52-53 52-55 53-54

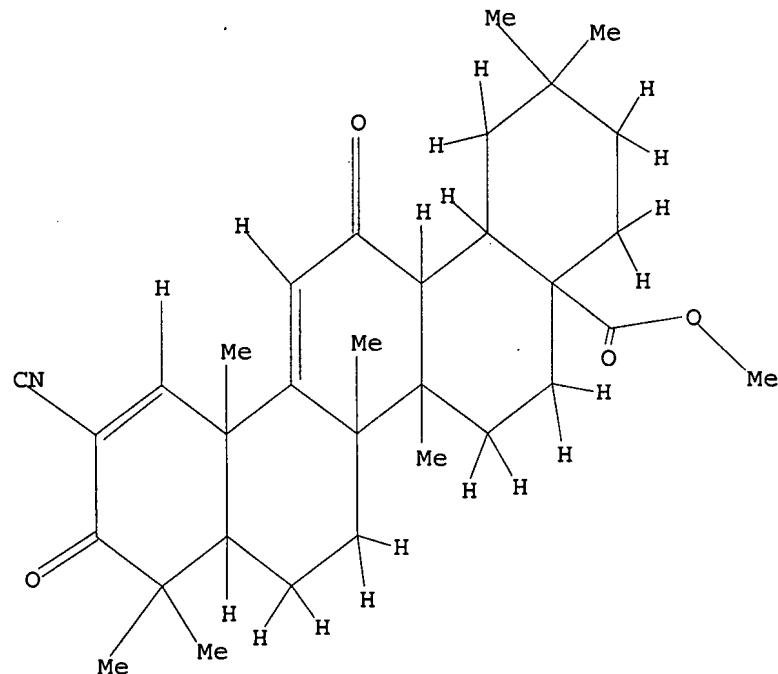
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ring bonds :  
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 13-14 13-15 14-18 15-16 15-19 16-17 16-22 17-18 19-20 20-21 21-22  
 exact/norm bonds :  
 1-2 1-6 2-3 2-23 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-14 9-10 11-12  
 12-13 12-32 13-14 13-15 14-18 15-16 15-19 16-17 16-22 17-18 19-20 20-21  
 21-22 52-53 52-55  
 exact bonds :  
 1-25 1-26 3-24 4-33 5-27 6-34 8-28 9-37 9-38 10-35 10-36 11-45 13-44  
 14-29 15-43 16-52 17-41 17-42 18-39 18-40 19-46 19-47 20-30 20-31 21-48  
 21-49 22-50 22-51 53-54

Match level :  
 1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
 11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom  
 20:Atom 21:Atom 22:Atom 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS  
 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS  
 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS  
 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS  
 52:CLASS 53:CLASS 54:CLASS 55:CLASS

L1 STRUCTURE UPLOADED

=> d 11  
 L1 HAS NO ANSWERS  
 L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 11  
 SAMPLE SEARCH INITIATED 11:41:47 FILE 'REGISTRY'  
 SAMPLE SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED

7 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 7 TO 298  
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s 11 full  
FULL SEARCH INITIATED 11:41:51 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 113 TO ITERATE

100.0% PROCESSED 113 ITERATIONS  
SEARCH TIME: 00.00.01

2 ANSWERS

L3 2 SEA SSS FUL L1

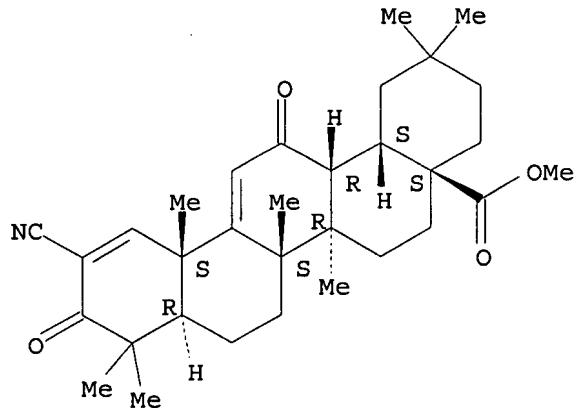
=> d 13

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2007 ACS on STN  
RN 418764-26-8 REGISTRY  
ED Entered STN: 20 May 2002  
CN Oleana-1,9(11)-dien-28-oic acid, 2-cyano-3,12-dioxo-, methyl ester, compd.  
with methanol (1:1), monohydrate (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C32 H43 N O4 . C H4 O . H2 O  
SR CA  
LC STN Files: CA, CAPLUS, IMSRESEARCH

CM 1

CRN 218600-53-4  
CMF C32 H43 N O4

Absolute stereochemistry. Rotation (+).



CM 2

CRN 67-56-1  
CMF C H4 O

H<sub>3</sub>C—OH

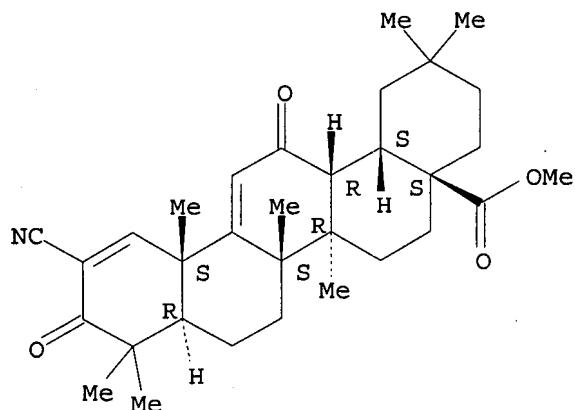
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d scan

L3 2 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN  
IN Oleana-1,9(11)-dien-28-oic acid, 2-cyano-3,12-dioxo-, methyl ester  
MF C32 H43 N O4  
CI COM

Absolute stereochemistry. Rotation (+).



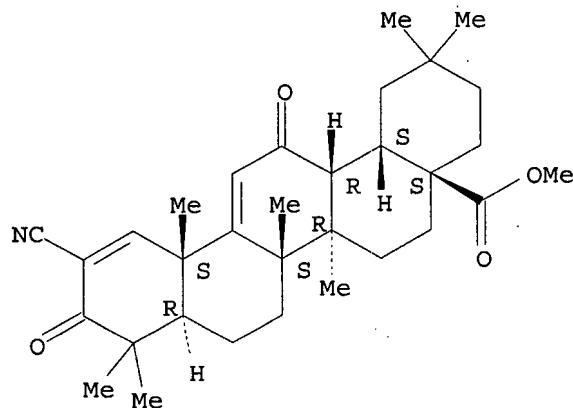
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 2 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN  
IN Oleana-1,9(11)-dien-28-oic acid, 2-cyano-3,12-dioxo-, methyl ester, compd.  
with methanol (1:1), monohydrate (9CI)  
MF C32 H43 N O4 . C H4 O . H2 O

CM 1

Absolute stereochemistry. Rotation (+).



CM 2

H<sub>3</sub>C—OH

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> file medline caplus wpids uspatfull  
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	174.50	174.71

FILE 'MEDLINE' ENTERED AT 11:42:29 ON 07 NOV 2007

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=> s 13

SAMPLE SEARCH INITIATED 11:42:34 FILE 'WPIDS'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 0 TO 0

PROJECTED ANSWERS: 0 TO 0

L4 30 L3

=> s 14 and (cancer or tumor)

L5 20 L4 AND (CANCER OR TUMOR)

=> d 15 1-20 ibib, abs

L5 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:508813 CAPLUS

DOCUMENT NUMBER: 147:157653

TITLE: The novel triterpenoid C-28 methyleEster of 2-cyano-3,  
12-dioxoolen-1, 9-dien-28-oic acid inhibits metastatic  
murine breast tumor growth through  
inactivation of STAT3 signaling

AUTHOR(S): Ling, Xiaoyang; Konopleva, Marina; Zeng, Zhihong;  
Ruvolo, Vivian; Stephens, L. Clifton; Schober, Wendy;  
McQueen, Teresa; Dietrich, Martin; Madden, Timothy L.;  
Andreeff, Michael

CORPORATE SOURCE: Section of Molecular Hematology and Therapy,  
Department of Stem Cell Transplantation and Cellular

SOURCE:

Therapy, The University of Texas M. D. Anderson Cancer Center, Houston, TX, USA

Cancer Research (2007), 67(9), 4210-4218

CODEN: CNREA8; ISSN: 0008-5472

American Association for Cancer Research

PUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

AB We and others have reported that C-28 Me ester of 2-cyano-3, 12-dioxoolen-1, 9-dien-28-oic acid (CDDO-Me) effectively inhibits the growth of multiple cancer cell types. Our previous studies indicated that prolonged CDDO-Me treatment inactivated extracellular signal-regulated kinase signaling in acute myelogenous leukemia cells. Whether treatment with CDDO-Me has an earlier effect on other proteins that are important for either signal transduction or oncogenesis is unknown. Constitutively activated signal transducer and activator of transcription 3 (STAT3) is frequently found in human breast cancer samples. Constitutively activated STAT3 was shown to up-regulate c-Myc in several types of cancer and has a feedback effect on Src and Akt. To examine the effects of CDDO-Me on STAT3 signaling in breast cancer, we used the murine 4T1 breast tumor model, which is largely resistant to chemotherapy. In vitro, after treatment of 4T1 cells with 500 nmol/L CDDO-Me for 2 h, we found (a) inactivation of STAT3, (b) inactivation of Src and Akt, (c) 4-fold reduction of c-Myc mRNA levels, (d) accumulation of cells in G2-M cell cycle phase, (e) abrogation of invasive growth of 4T1 cells, and (f) lack of apoptosis induction. In in vivo studies, CDDO-Me completely eliminated 4T1 breast cancer growth and lung metastases induced by 4T1 cells in mice when treatment started 1 day after tumor implantation and significantly inhibited tumor growth when started after 5 days. In vivo studies also indicated that splenic mature dendritic cells were restored after CDDO-Me treatment. In summary, these data suggest that CDDO-Me may have therapeutic potential in breast cancer therapy, in part, through inactivation of STAT3.

REFERENCE COUNT:

33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2007:289385 CAPLUS

DOCUMENT NUMBER: 146:492789

TITLE: The Synthetic Triterpenoids CDDO-Methyl Ester and CDDO-Ethyl Amide Prevent Lung Cancer Induced by Vinyl Carbamate in A/J Mice

AUTHOR(S): Liby, Karen; Royce, Darlene B.; Williams, Charlotte R.; Risingsong, Renee; Yore, Mark M.; Honda, Tadashi; Gribble, Gordon W.; Dmitrovsky, Ethan; Sporn, Thomas A.; Sporn, Michael B.

CORPORATE SOURCE: Department of Pharmacology, Dartmouth Med. Sch., Dartmouth Coll., Hanover, NH, USA

SOURCE: Cancer Research (2007), 67(6), 2414-2419

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We report the first use of new synthetic triterpenoids to prevent lung cancer in exptl. animals. Female A/J mice were treated with the mutagenic carcinogen vinyl carbamate, which induces adenocarcinoma of the lung in all animals within 16 wk. If mice were fed either the Me ester or the Et amide derivative of the synthetic triterpenoid 2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oic acid (CDDO-ME and CDDO-EA, resp.), beginning 1 wk after dosing with carcinogen, the number, size, and severity of lung carcinomas were markedly reduced. The mechanisms of action of CDDO-ME and CDDO-EA that are germane to these in vivo findings are the following results shown here in cell culture: (a) suppression of the ability of IFN- $\gamma$  to induce de novo formation of nitric oxide synthase in a macrophage-like cell line RAW264.7, (b) induction of heme oxygenase-1 in

these RAW cells, and (c) suppression of phosphorylation of the transcription factor signal transducers and activators of transcription 3 as well as induction of apoptosis in human lung cancer cell lines.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2006:1323361 CAPLUS  
DOCUMENT NUMBER: 146:308789  
TITLE: The synthetic triterpenoid 1-[2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oyl]imidazole blocks nuclear factor- $\kappa$ B activation through direct inhibition of  $\text{I}\kappa\text{B}$  kinase  $\beta$   
AUTHOR(S): Yore, Mark M.; Liby, Karen T.; Honda, Tadashi; Gribble, Gordon W.; Sporn, Michael B.  
CORPORATE SOURCE: Department of Pharmacology, Dartmouth Medical School and Department of Chemistry, Dartmouth College, Hanover, NH, USA  
SOURCE: Molecular Cancer Therapeutics (2006), 5(12), 3232-3239  
CODEN: MCTOCE ISSN: 1535-7163  
PUBLISHER: American Association for Cancer Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The synthetic triterpenoid 1-[2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oyl]imidazole (CDDO-Im) is a multifunctional agent with potent anti-inflammatory, antiproliferative, cytoprotective, and apoptotic activities, whose mol. targets are unknown. Using both cell-free and cellular assays, we show that CDDO-Im is a direct inhibitor of  $\text{I}\kappa\text{B}$  kinase (IKK) $\beta$  and that it thereby inhibits binding of nuclear factor- $\kappa$ B to DNA and subsequent transcriptional activation. Pretreatment of cells with CDDO-Im prevents  $\text{I}\kappa\text{B}\alpha$  phosphorylation and degradation in response to tumor necrosis factor  $\alpha$ . The kinetics of this inhibition by CDDO-Im are rapid and occur within 15 min. A biotinylated analog of CDDO-Im showed that CDDO-Im binds to the IKK signalsome. Furthermore, we show that Cys179 on IKK is a target for CDDO-Im. This is the first report to show that this novel synthetic triterpenoid binds to and inhibits IKK $\beta$  directly.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2006:1220460 CAPLUS  
DOCUMENT NUMBER: 146:134811  
TITLE: Triterpenoid CDDO-Me blocks the NF- $\kappa$ B pathway by direct inhibition of IKK $\beta$  on cys-179  
AUTHOR(S): Ahmad, Rehan; Raina, Deepak; Meyer, Colin; Kharbanda, Surender; Kufe, Donald  
CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA  
SOURCE: Journal of Biological Chemistry (2006), 281(47), 35764-35769  
CODEN: JBCHA3 ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The novel oleanane triterpenoid 2-cyano-3,12-dioxooleana-1,9,-dien-28-oic acid (CDDO) and the C-28 Me ester (CDDO-Me) induce apoptosis of human tumor cells by disruption of redox balance and are currently in clin. trials. The present studies show that CDDO and CDDO-Me block tumor necrosis factor $\alpha$ -induced targeting of NF- $\kappa$ B p65 to the nucleus. CDDO-Me also blocked tumor necrosis factor $\alpha$ -induced phosphorylation of  $\text{I}\kappa\text{B}\alpha$ . In concert with these results, we found that CDDO-Me inhibits  $\text{I}\kappa\text{B}\alpha$

kinase $\beta$  (IKK $\beta$ ) activity in cells. In support of a direct mechanism, CDDO-Me inhibited recombinant IKK $\beta$  activity in vitro. The results also demonstrate that (i) CDDO and CDDO-Me form adducts with IKK $\beta$ , but not IKK $\beta$  with mutation of Cys-179 to Ala, and (ii) CDDO-Me inhibits IKK $\beta$  by a mechanism dependent on oxidation of Cys-179. These findings indicate that CDDO and CDDO-Me directly block IKK $\beta$  activity and thereby the NF- $\kappa$ B pathway by interacting with Cys-179 in the IKK $\beta$  activation loop.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:823024 CAPLUS

DOCUMENT NUMBER: 146:220301

TITLE: Depletion of intracellular glutathione contributes to JNK-mediated death receptor 5 upregulation and apoptosis induction by the novel synthetic triterpenoid methyl-2-cyano-3, 12-dioxooleana-1, 9-dien-28-oate (CDDO-Me)

AUTHOR(S): Yue, Ping; Zhou, Zhongmei; Khuri, Fadlo R.; Sun, Shi-Yong

CORPORATE SOURCE: Department of Hematology and Oncology; Winship Cancer Institute, Emory University School of Medicine, Atlanta, GA, USA

SOURCE: Cancer Biology & Therapy (2006), 5(5), 492-497

CODEN: CBTAAO; ISSN: 1538-4047

PUBLISHER: Landes Bioscience

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The novel synthetic triterpenoid methyl-2-cyano-3, 12-dioxooleana-1, 9-dien-28-oate (CDDO-Me) induces apoptosis in human cancer cells, showing potential as a cancer therapeutic agent. We previously demonstrated that CDDO-Me induces a c-Jun N-terminal kinase (JNK)-mediated DR5 expression and apoptosis. This study revealed the mechanism by which CDDO-Me induces JNK activation and subsequent DR5 upregulation and apoptosis. To determine whether CDDO-Me activates JNK and induces DR5 expression and apoptosis via oxidative stress by inducing the generation of reactive oxygen species (ROS), we examined the effects of various antioxidants on JNK activation, DR5 upregulation, and apoptosis induction by CDDO-Me. Thiol antioxidants, including N-acetyl-L-cysteine (NAC), glutathione (GSH) and dithiothreitol (DTT), abrogated CDDO-Me-induced apoptosis. In contrast, nonthiol antioxidants, including butylated hydroxyanisole (BHA), Trolox, mannitol, and Mn(II) tetra(4-benzoic acid) porphyrin chloride (MnTBAP), failed to do so, with the exception of vitamin C (Vit C). Accordingly, only thiol antioxidants blocked JNK activation induced by CDDO-Me. CDDO-Me reduced intracellular levels of GSH; this reduction was abrogated only by thiol antioxidants and Vit C. However, CDDO-Me did not promote ROS generation. These results suggest that depletion of intracellular GSH, but not ROS generation, contributes to CDDO-Me-induced JNK activation and apoptosis, at least in our systems. Furthermore, these thiol antioxidants abrogated CDDO-Me-induced DR5 expression, whereas the GSH-depleting agent diethylmaleate also upregulated DR5 expression at concns. that deplete intracellular GSH, demonstrating that GSH depletion can cause DR5 upregulation. Collectively, we conclude that CDDO-Me activates the JNK pathway via depletion of intracellular GSH, leading to DR5 upregulation and induction of apoptosis.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:264028 CAPLUS

DOCUMENT NUMBER: 145:262581

TITLE: A Synthetic Triterpenoid, CDDO-Me, Inhibits I $\kappa$ B $\alpha$  Kinase and Enhances Apoptosis Induced

by TNF and Chemotherapeutic Agents through  
Down-Regulation of Expression of Nuclear Factor  
κB-Regulated Gene Products in Human Leukemic  
Cells

AUTHOR(S): Shishodia, Shishir; Sethi, Gautam; Konopleva, Marina; Andreeff, Michael; Aggarwal, Bharat B.  
CORPORATE SOURCE: Cytokine Research Laboratory, Department of Experimental Therapeutics and Section of Molecular Hematology and Therapy, Department of Blood and Marrow Transplantation, The University of Texas M.D. Anderson Cancer Center, Houston, TX, USA  
SOURCE: Clinical Cancer Research (2006), 12(6), 1828-1838  
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The C-28 Me ester of 2-cyano-3,12-dioxoolean-1,9-dien-28-oic acid (CDDO-Me), a synthetic triterpenoid based on naturally occurring ursolic and oleanolic acids, induces apoptosis in tumor cells, induces differentiation, and inhibits inflammatory response through a poorly understood mechanism. Because the nuclear transcription factor nuclear factor κB (NF-κB) has been shown to suppress apoptosis and promote proliferation and is linked with inflammation and differentiation, we postulated that CDDO-Me modulates NF-κB activity and NF-κB-regulated gene expression. Using human leukemia cell lines and patient samples, we show that CDDO-Me potently inhibits both constitutive and inducible NF-κB activated by tumor necrosis factor (TNF), interleukin (IL)-1 $\beta$ , phorbol ester, okadaic acid, hydrogen peroxide, lipopolysaccharide, and cigarette smoke. CDDO-Me was more potent than CDDO and its imidazole derivative NF-κB suppression occurred through inhibition of I $\kappa$ B $\alpha$  kinase activation, I $\kappa$ B $\alpha$  phosphorylation, I $\kappa$ B $\alpha$  degradation, p65 phosphorylation, p65 nuclear translocation, and NF-κB-mediated reporter gene transcription. This inhibition correlated with suppression of NF-κB-dependent genes involved in antiapoptosis (IAP2, cFLIP, TRAF1, survivin, and bcl-2), proliferation (cyclin d1 and c-myc), and angiogenesis (VEGF, cox-2, and mmp-9). CDDO-Me also potentiated the cytotoxic effects of TNF and chemotherapeutic agents. Overall, our results suggest that CDDO-Me inhibits NF-κB through inhibition of I $\kappa$ B $\alpha$  kinase, leading to the suppression of expression of NF-κB-regulated gene products and enhancement of apoptosis induced by TNF and chemotherapeutic agents.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:580980 CAPLUS

DOCUMENT NUMBER: 143:221979

TITLE: 2-Cyano-3,12-dioxoolean-1,9-dien-28-oic acid and related compounds inhibit growth of colon cancer cells through peroxisome proliferator-activated receptor  $\gamma$ -dependent and -independent pathways

AUTHOR(S): Chintharlapalli, Sudhakar; Papineni, Sabitha; Konopleva, Marina; Andreef, Michael; Samudio, Ismael; Safe, Stephen

CORPORATE SOURCE: Department of Biochemistry and Biophysics, Texas A and M University, College Station, TX, USA

SOURCE: Molecular Pharmacology (2005), 68(1), 119-128

CODEN: MOPMA3; ISSN: 0026-895X  
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB 2-Cyano-3,12-dioxoolean-1,9-dien-28-oic acid (CDDO) and the corresponding

Me (CDDO-Me) and imidazole (CDDO-Im) esters induce peroxisome proliferator-activated receptor  $\gamma$  (PPAR $\gamma$ )-dependent transactivation in SW-480 colon cancer cells, and these responses were inhibited by small inhibitory RNA for PPAR $\gamma$ . Moreover, in a mammalian two-hybrid assay using the PPAR $\gamma$ 2-VP16 fusion plasmid and GAL4-coactivator/corepressor chimeras and a construct (pGAL4) containing five tandem GAL4 response elements, CDDO, CDDO-Me, and CDDO-IM induce transactivation and PPAR $\gamma$  interaction with multiple coactivators. A major difference among the three PPAR $\gamma$  agonists was the higher activity of CDDO-Im to induce PPAR $\gamma$  interactions with the corepressor SMRT. CDDO, CDDO-Me, and CDDO-Im inhibited SW-480, HCT-116, and HT-29 colon cancer cell proliferation at low concns. and induced cell death at higher concns. Growth inhibition at lower concns. correlated with induction of the tumor suppressor gene caveolin-1 which is known to inhibit colon cancer cell growth. Induction of caveolin-1 by CDDO, CDDO-Me, and CDDO-Im was inhibited by the PPAR $\gamma$  antagonist N-4'-aminopyridyl-2-chloro-5-nitrobenzamide (T007), whereas higher doses induced apoptosis [poly(ADP-ribose) polymerase cleavage], which was not inhibited by T007. These results illustrate that CDDO-, CDDO-Me, and CDDO-Im induce both PPAR $\gamma$ -dependent and -independent responses in colon cancer cells, and activation of these pathways are separable and concentration-dependent for all three compds.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:480865 CAPLUS

DOCUMENT NUMBER: 143:166163

TITLE: Triterpenoid CDDO-Im downregulates PML/RAR $\alpha$

expression in acute promyelocytic leukemia cells

Ikeda, T.; Kimura, F.; Nakata, Y.; Sato, K.; Ogura, K.; Motoyoshi, K.; Sporn, M.; Kufe, D.

CORPORATE SOURCE: Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Cell Death and Differentiation (2005), 12(5), 523-531

CODEN: CDEIEK; ISSN: 1350-9047

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The triterpenoid 2-cyano-3,12-dioxooleana-1,9-dien-28-oic acid (CDDO) induces differentiation and apoptosis of diverse human tumor cells. In the present study, we examined the effects of the CDDO imidazolide imide (CDDO-Im) on the NB4 acute promyelocytic leukemia (APL) cell line and primary APL cells. The results show that CDDO-Im selectively downregulates expression of the PML/retinoic receptor alpha fusion protein by a caspase-dependent mechanism and sensitizes APL cells to the differentiating effects of all-trans retinoic acid (ATRA). CDDO-Im treatment of APL cells was also associated with disruption of redox balance and activation of the extrinsic apoptotic pathway. In concert with these results, CDDO-Im sensitizes APL cells to arsenic trioxide (ATO)-induced apoptosis. Our findings indicate that CDDO-Im may be effective in the treatment of APL by: (i) downregulation of PML/RAR $\alpha$ ; (ii) enhancement of ATRA-induced differentiation; and (iii) sensitization of ATO-induced APL cell death.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:670953 CAPLUS

DOCUMENT NUMBER: 141:342861

TITLE: Design, Synthesis, and Biological Evaluation of Biotin Conjugates of 2-Cyano-3,12-dioxooleana-1,9(11)-dien-28-oic Acid for the Isolation of the Protein Targets

AUTHOR(S): Honda, Tadashi; Janosik, Tomasz; Honda, Yukiko; Han, Jie; Liby, Karen T.; Williams, Charlotte R.; Couch,

Robin D.; Anderson, Amy C.; Sporn, Michael B.;  
Gribble, Gordon W.  
CORPORATE SOURCE: Department of Chemistry, Dartmouth College, Hanover,  
NH, 03755, USA  
SOURCE: Journal of Medicinal Chemistry (2004), 47(20),  
4923-4932  
PUBLISHER: CODEN: JMCMAR; ISSN: 0022-2623  
American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 141:342861  
AB 2-Cyano-3,12-dioxoolean-1,9(11)-dien-28-oic acid (CDDO) and related  
compds. [for example, CDDO-Me and CDDO-Im] are potential  
anti-inflammatory, cancer chemopreventive, and chemotherapeutic  
agents. However, the mechanisms responsible for the multiple effects of  
CDDO are still unclear. Clarification of these mechanisms and  
particularly isolation of the protein targets are essential for the  
development of CDDO and its analogs as clin. useful drugs. Such knowledge  
would provide superior opportunities for designing new compds. with  
improved potency and selectivity. Therefore, to isolate protein targets  
using affinity chromatog. with immobilized streptavidin as a carrier, we  
have designed and synthesized C-17 and C-23 biotin conjugates of CDDO on  
the basis of our established structure-activity relationships. For the  
synthesis of one compound, a new important precursor, 23-hydroxy-CDDO-Me  
was synthesized from 20 by a C-23 oxidation protocol, which involves  
cyclopalladation of the C-4 Me group from a 3-one oxime. The inhibitory  
activity of C-23 conjugate is only about 3 times less potent than the  
mother compound, CDDO, against the proliferation of MCF-7 breast  
cancer cells. Consequently, it may be a very promising tool for  
the isolation of the protein targets of CDDO.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2003:832882 CAPLUS  
DOCUMENT NUMBER: 140:399426  
TITLE: Synthetic triterpenoids activate a pathway for  
apoptosis in AML cells involving downregulation of  
FLIP and sensitization to TRAIL  
AUTHOR(S): Suh, W.-S.; Kim, Y. S.; Schimmer, A. D.; Kitada, S.;  
Minden, M.; Andreeff, M.; Suh, N.; Sporn, M.; Reed, J.  
C.  
CORPORATE SOURCE: The Burnham Institute, La Jolla, CA, 92037, USA  
SOURCE: Leukemia (2003), 17(11), 2122-2129  
PUBLISHER: Nature Publishing Group  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Acute myelogenous leukemia (AML) remains a deadly disease for most adult  
patients, due primarily to the emergence of chemoresistant cells. Defects  
in apoptosis pathways make important contributions to chemoresistance,  
suggesting a need to restore apoptosis sensitivity or to identify  
alternative pathways for apoptosis induction. Triterpenoids represent a  
class of naturally occurring and synthetic compds. with demonstrated  
antitumor activity, including 2-cyano-3,12-dioxoolean-1,9-dien-28-oic acid  
(CDDO) and its Me ester (CDDO-m). We explored the effects of CDDO and  
CDDO-m in vitro on established AML cell lines (HL-60, U937, AML-2) and on  
freshly isolated AML blasts. CDDO and CDDO-m reduced the viability of all  
AML cell lines tested in a dose-dependent manner, with ED<sub>50</sub>s for killing 50%  
of cells (ED<sub>50</sub>) within 48 h of apprx. 1 and 0.5 μM, resp. CDDO or  
CDDO-m also induced substantial increases in cell death in five out of 10  
samples of primary AML blasts. Cell death induced by CDDO and CDDO-m was  
attributed to apoptosis, based on characteristic cell morphol. and  
evidence of caspase activation. Immunoblot anal. demonstrated proteolytic  
processing of caspase-3, -7, and -8, but not caspase-9, suggesting the

involvement of the extrinsic' pathway, linked to apoptosis induction by TNF-family death receptors. Accordingly, CDDO and CDDO-m induced concentration-dependent redns. in the levels of FLIP protein, an endogenous antagonist of caspase-8, without altering the levels of several other apoptosis-relevant proteins. Redns. in FLIP were rapid, detectable within 3 h after exposure of AML cell lines to CDDO or CDDO-m. CDDO and CDDO-m also sensitized two of four leukemia lines to TRAIL, a TNF-family death ligand. The findings suggest that synthetic triterpenoids warrant further investigation in the treatment of AML, alone or in combination with TRAIL or other immune-based therapies.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:505732 CAPLUS

DOCUMENT NUMBER: 138:66283

TITLE: An inducible pathway for degradation of FLIP protein sensitizes tumor cells to TRAIL-induced apoptosis.

AUTHOR(S): Kim, Youngsoo; Suh, Nanjoo; Sporn, Michael; Reed, John C.

CORPORATE SOURCE: Burnham Institute, La Jolla, CA, 92037, USA

SOURCE: Journal of Biological Chemistry (2002), 277(25), 22320-22329

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB TRAIL (Apo2 ligand) is a member of the tumor necrosis factor (TNF) family of cytokines that induces apoptosis. Because TRAIL preferentially kills tumor cells, sparing normal tissues, interest has emerged in applying this biol. factor for cancer therapy in humans. However, not all tumors respond to TRAIL, raising questions about resistance mechanisms. We demonstrate here that a variety of natural and synthetic ligands of peroxisome proliferator-activated receptor- $\gamma$  (PPAR $\gamma$ ) sensitize tumor but not normal cells to apoptosis induction by TRAIL. PPAR $\gamma$  ligands selectively reduce levels of FLIP, an apoptosis-suppressing protein that blocks early events in TRAIL/TNF family death receptor signaling. Both PPAR $\gamma$  agonists and antagonists displayed these effects, regardless of the levels of PPAR $\gamma$  expression and even in the presence of a PPAR $\gamma$  dominant-neg. mutant, indicating a PPAR $\gamma$ -independent mechanism. Redns. in FLIP and sensitization to TRAIL-induced apoptosis were also not correlated with NF- $\kappa$ B, further suggesting a novel mechanism. PPAR $\gamma$  modulators induced ubiquitination and proteasome-dependent degradation of FLIP, without concomitant redns. in FLIP mRNA. The findings suggest the existence of a pharmacol. regulated novel target of this class of drugs that controls FLIP protein turnover, and raise the possibility of combining PPAR $\gamma$  modulators with TRAIL for more efficacious elimination of tumor cells through apoptosis.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:465747 CAPLUS

DOCUMENT NUMBER: 137:41724

TITLE: CDDO (2-cyano-3,12-dioxoolean-1,9-dien-28-oic acid)

compounds and combinations with other chemotherapeutics for the treatment of cancer and graft vs. host disease

INVENTOR(S): Konopleva, Marina; Andreeff, Michael; Sporn, Michael

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA

SOURCE: PCT Int. Appl., 184 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002047611	A2	20020620	WO 2001-US44541	20011128
WO 2002047611	A8	20030626		
WO 2002047611	A3	20031224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2430454	A1	20020620	CA 2001-2430454	20011128
AU 2002043246	A5	20020624	AU 2002-43246	20011128
US 2003119732	A1	20030626	US 2001-998009	20011128
EP 1395255	A2	20040310	EP 2001-989130	20011128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-253673P P 20001128  
WO 2001-US44541 W 20011128

AB CDDO compds. in combination with other chemotherapeutic agents induce and potentiate cytotoxicity and apoptosis in cancer cells. One class of chemotherapeutic agents include retinoids. Cancer therapies based on these combination therapies are provided. Also provided are methods to treat graft vs. host diseases using the CDDO compds.

L5 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:95270 CAPLUS  
DOCUMENT NUMBER: 136:379616  
TITLE: Identification of a novel synthetic triterpenoid, methyl-2-cyano-3,12-dioxooleana-1,9-dien-28-oate, that potently induces caspase-mediated apoptosis in human lung cancer cells  
AUTHOR(S): Kim, Kevin B.; Lotan, Reuben; Yue, Ping; Sporn, Michael B.; Suh, Nanjoo; Gribble, Gordon W.; Honda, Tadashi; Wu, Gen Sheng; Hong, Waun Ki; Sun, Shi-Yong  
CORPORATE SOURCE: Department of Thoracic/Head and Neck Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA  
SOURCE: Molecular Cancer Therapeutics (2002), 1(3), 177-184  
CODEN: MCTOCF; ISSN: 1535-7163  
PUBLISHER: American Association for Cancer Research  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Lung cancer continues to be the leading cause of cancer-related death in the United States. Therefore, new agents targeting prevention and treatment of lung cancer are urgently needed. In the present study, we demonstrate that a novel synthetic triterpenoid methyl-2-cyano-3,12-dioxooleana-1,9-dien-28-oate (CDDO-Me) is a potent inducer of apoptosis in human non-small cell lung carcinoma (NSCLC) cells. The concns. required for a 50% decrease in cell survival (IC50) ranged from 0.1 to 0.3  $\mu$ M. CDDO-Me induced rapid apoptosis and triggered a series of effects associated with apoptosis including a rapid release of cytochrome c from mitochondria, activation of procaspase-9, -7, -6, and -3, and cleavage of poly(ADP-ribose) polymerase and lamin A/C. Moreover, the caspase-3 inhibitor Z-DEVD-FMK and the pan caspase inhibitor Z-VAD-FMK

suppressed CDDO-Me-induced apoptosis. These results indicate that CDDO-Me induced apoptosis in human NSCLC cells via a cytochrome c-triggered caspase activation pathway. CDDO-Me did not alter the level of Bcl-2 and Bcl-xL proteins, and no correlation was found between cell sensitivity to CDDO-Me and basal Bcl-2 expression level. Furthermore, overexpression of Bcl-2 did not protect cells from CDDO-Me-induced apoptosis. These results suggest that CDDO-Me induces apoptosis in NSCLC cells irresp. of Bcl-2 expression level. In addition, no correlation was found between cell sensitivity to CDDO-Me and p53 status, suggesting that CDDO-Me induce a p53-independent apoptosis. Our results demonstrate that CDDO-Me may be a good candidate for addnl. evaluation as a potential therapeutic agent for human lung cancers and possibly other types of cancer.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:632697 CAPLUS

DOCUMENT NUMBER: 133:350364

TITLE: Synthetic Oleanane and Ursane Triterpenoids with Modified Rings A and C: A Series of Highly Active Inhibitors of Nitric Oxide Production in Mouse Macrophages

AUTHOR(S): Honda, Tadashi; Rounds, BarbieAnn V.; Bore, Lothar; Finlay, Heather J.; Favaloro, Frank G. ,Jr.; Suh, Nanjoo; Wang, Yongping; Sporn, Michael B.; Gribble, Gordon W.

CORPORATE SOURCE: Department of Chemistry, Dartmouth College Dartmouth Medical School, Hanover, NH, 03755, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(22), 4233-4246

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 133:350364

AB New olean- and urs-1-en-3-one triterpenoids with various modified rings C have been synthesized as potential antiinflammatory and cancer chemopreventive agents and evaluated for their inhibitory activities against production of nitric oxide induced by interferon- $\gamma$  in mouse macrophages. These studies revealed that 9(11)-en-12-one and 12-en-11-one functionalities in ring C increase the potency by about 2-10 times compared with the original 12-ene. Subsequently, novel olean- and urs-1-en-3-one derivs. with nitrile and carboxyl groups at C-2 in ring A and with 9(11)-en-12-one and 12-en-11-one functionalities in ring C were synthesized. Among them, Me 2-cyano-3, 12-dioxooleana-1,9(11)-dien-28-oate, 2-cyano-3,12-dioxooleana-1,9(11)-dien-28-oic acid (CDDO) (I), and Me 2-carboxy-3,12-dioxooleana-1,9(11)-dien-28-oate were found to have extremely high potency (IC<sub>50</sub> = 0.1 nM level). Their potency is similar to that of dexamethasone although they do not act through the glucocorticoid receptor. Overall, the combination of modified rings A and C increases the potency by about 10 000 times compared with the lead compound, 3-oxooleana-1,12-dien-28-oic acid (IC<sub>50</sub> = 1  $\mu$ M level). The selected oleanane triterpenoid, I, was found to be a potent, multifunctional agent in various in vitro assays and to show antiinflammatory activity against thioglycollate-interferon- $\gamma$ -induced mouse peritonitis.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:811070 CAPLUS

DOCUMENT NUMBER: 132:44971

TITLE: Therapeutic triterpenoid compositions and methods of use for treatment of cancer, neurodegenerative, diseases, and inflammatory bowel diseases

INVENTOR(S): Gribble, Gordon W.; Honda, Tadashi; Sporn, Michael B.;  
 Suh, Nanjoo  
 PATENT ASSIGNEE(S): Trustees of Dartmouth College, USA  
 SOURCE: PCT Int. Appl., 49 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965478	A1	19991223	WO 1999-US13635	19990618
W: CA, JP RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6326507	B1	20011204	US 1999-335003	19990617
CA 2335505	A1	19991223	CA 1999-2335505	19990618
EP 1089724	A1	20010411	EP 1999-928731	19990618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002530272	T	20020917	JP 2000-554358	19990618
US 2002042535	A1	20020411	US 2001-927081	20010809
US 6552075	B2	20030422		
US 2003236303	A1	20031225	US 2003-395372	20030324
US 7288568	B2	20071030		
US 2005288363	A1	20051229	US 2005-121316	20050503
PRIORITY APPLN. INFO.:			US 1998-90053P	P 19980619
			US 1999-335003	A 19990617
			WO 1999-US13635	W 19990618
			US 2001-927081	A1 20010809
			US 2003-395372	A1 20030324

OTHER SOURCE(S): MARPAT 132:44971  
 AB Triterpenoid compds., e.g. 2-cyano-3,12-dioxoolean-1,9-dien--28-oic acid, and methods are disclosed which are useful for chemopreventative treatment of diseases such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 20 USPATFULL on STN  
 ACCESSION NUMBER: 2005:331377 USPATFULL  
 TITLE: Therapeutic compositions and methods of use  
 INVENTOR(S): Gribble, Gordon W., Norwich, VT, UNITED STATES  
 Honda, Tadashi, Hanover, NH, UNITED STATES  
 Sporn, Michael B., Tunbridge, VT, UNITED STATES  
 Suh, Nanjoo, Hanover, NH, UNITED STATES  
 PATENT ASSIGNEE(S): Trustees of Dartmouth College (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005288363	A1	20051229
APPLICATION INFO.:	US 2005-121316	A1	20050503 (11)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2003-395372, filed on 24 Mar 2003, PENDING		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	FULBRIGHT & JAWORSKI L.L.P., 600 CONGRESS AVE., SUITE 2400, AUSTIN, TX, 78701, US		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	11 Drawing Page(s)		
LINE COUNT:	931		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
AB	Compounds and methods useful for chemopreventative treatment of diseases		

such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 17 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2003:335425 USPATFULL

TITLE: Therapeutic compositions and methods of use

INVENTOR(S): Gribble, Gordon W., Norwich, VT, UNITED STATES

Honda, Tadashi, Hanover, NH, UNITED STATES

Sporn, Michael B., Tunbridge, VT, UNITED STATES

Sun, Nanjoo, Hanover, NH, UNITED STATES

PATENT ASSIGNEE(S): Trustees of Dartmouth College (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2003236303 A1 20031225

US 7288568 B2 20071030

APPLICATION INFO.: US 2003-395372 A1 20030324 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-927081, filed on 9 Aug 2001, GRANTED, Pat. No. US 6552075 Division of Ser. No. US 1999-335003, filed on 17 Jun 1999, GRANTED, Pat. No. US 6326507

NUMBER DATE

PRIORITY INFORMATION: US 1998-90053P 19980619 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Steven L. Highlander, Esq., FULBRIGHT & JAWORSKI L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701

NUMBER OF CLAIMS: 73

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 14 Drawing Page(s)

LINE COUNT: 1146

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds and methods useful for chemopreventative treatment of diseases such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INSTANT APP.

L5 ANSWER 18 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2003:173884 USPATFULL

TITLE: CDDO-compounds and combination therapies thereof

INVENTOR(S): Konopleva, Marina, Houston, TX, UNITED STATES

Andreeff, Michael, Houston, TX, UNITED STATES

Sporn, Michael B., Tunbridge, VT, UNITED STATES

PATENT ASSIGNEE(S): Board of (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2003119732 A1 20030626

APPLICATION INFO.: US 2001-998009 A1 20011128 (9)

NUMBER DATE

PRIORITY INFORMATION: US 2000-253673P 20001128 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Priya D. Subramony, Fulbright & Jaworski L.L.P., 600 Congress Avenue, Suite 2400, Austin, TX, 78701

NUMBER OF CLAIMS: 79

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 35 Drawing Page(s)

LINE COUNT: 5276

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB CDDO-compounds in combination with other chemotherapeutic agents induce and potentiate cytotoxicity and apoptosis in cancer cell. One class of chemotherapeutic agents include retinoids. Cancer therapies based on these combination therapies are provided. Also provided are methods to treat graft versus host diseases using the CDDO compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 19 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2002:78876 USPATFULL

TITLE: Therapeutic compounds and methods of use

INVENTOR(S): Gribble, Gordon W., Norwich, VT, UNITED STATES

Honda, Tadashi, Hanover, NH, UNITED STATES

Sporn, Michael B., Tunbridge, VT, UNITED STATES

Suh, Nanjoo, Hanover, NH, UNITED STATES

PATENT ASSIGNEE(S): Trustees of Dartmouth College (U.S. corporation)

NUMBER	KIND	DATE
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PATENT INFORMATION: US 2002042535 A1 20020411

US 6552075 B2 20030422

APPLICATION INFO.: US 2001-927081 A1 20010809 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1999-335003, filed on 17 Jun 1999, PENDING

NUMBER	DATE
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PRIORITY INFORMATION: US 1998-90053P 19980619 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Steven L. Highlander, FULBRIGHT & JAWORSKI L.L.P., Suite 2400, 600 Congress Avenue, Austin, TX, 78701

NUMBER OF CLAIMS: 73

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 11 Drawing Page(s)

LINE COUNT: 1150

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds and methods useful for chemopreventative treatment of diseases such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 20 OF 20 USPATFULL on STN

ACCESSION NUMBER: 2001:221178 USPATFULL

TITLE: Therapeutic compounds and methods of use

INVENTOR(S): Gribble, Gordon W., Norwich, VT, United States

Honda, Tadashi, Hanover, NH, United States

Sporn, Michael B., Tunbridge, VT, United States

Suh, Nanjoo, Hanover, NH, United States

PATENT ASSIGNEE(S): Trustees of Dartmouth College, Hanover, NH, United States (U.S. corporation)

NUMBER	KIND	DATE
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PATENT INFORMATION: US 6326507 B1 20011204

US 1999-335003 19990617 (9)

NUMBER	DATE
--------	------

PRIORITY INFORMATION: US 1998-90053P 19980619 (60)

DOCUMENT TYPE: Utility  
FILE SEGMENT: GRANTED  
PRIMARY EXAMINER: Higel, Floyd D.  
ASSISTANT EXAMINER: Sackey, Ebenezer  
LEGAL REPRESENTATIVE: Fulbright & Jaworski, LLP  
NUMBER OF CLAIMS: 13  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 11 Drawing Page(s)  
LINE COUNT: 964  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB Compounds and methods useful for chemopreventative treatment of diseases such as cancer, Alzheimer's disease, Parkinson's disease, inflammatory bowel diseases, and multiple sclerosis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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(FILE 'HOME' ENTERED AT 11:41:16 ON 07 NOV 2007)

FILE 'REGISTRY' ENTERED AT 11:41:28 ON 07 NOV 2007

L1 STRUCTURE uploaded  
L2 0 S L1  
L3 2 S L1 FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 11:42:29 ON 07 NOV 2007

L4 30 S L3  
L5 20 S L4 AND (CANCER OR TUMOR)

=>

---Logging off of STN---

=>  
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	63.44	238.15
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-11.70	-11.70

STN INTERNATIONAL LOGOFF AT 11:43:14 ON 07 NOV 2007